

1. An apparatus to prepare a biocompatible matrix from a matrix-forming fluid comprising
  - a chamber to contain a matrix-forming fluid, said chamber defined by at least a top planar surface of a heat conductive material and a bottom
  - 5 planar surface of a heat conductive material, said top and bottom surfaces effective to symmetrically remove heat from said top surface and said bottom surface of said matrix-forming fluid,
  - at least one gasket having a uniform thickness positioned between said top and bottom surfaces to define a perimeter of said chamber,
  - 10 said gasket capable of containing said matrix-forming fluid within said perimeter, and
  - a plurality of fasteners to fasten said apparatus.
2. The apparatus of claim 1 further comprising a container sized to contain a coolant fluid for immersion of said apparatus in said coolant fluid.
3. The apparatus of claim 2 wherein said container is open.
4. The apparatus of claim 1 wherein said chamber is a bladder.
5. The apparatus of claim 1 wherein said heat conductive material is a metal.

6. A method for producing a biocompatible matrix comprising containing a matrix-forming fluid within a chamber, said chamber having a perimeter defined by a gasket, a top surface of a thermal conductive material in contact with said fluid, and a bottom surface of a thermal conductive material in contact with said fluid,
  - 5 cooling said matrix-forming fluid under conditions to produce a matrix having substantially symmetric reticulations and uniform thickness, dehydrating the matrix, and physically crosslinking the matrix.
7. The method of claim 6 wherein physical crosslinking is by a method selected from the group consisting of thermal dehydration, gamma irradiation, and combinations thereof.
8. The method of claim 6 wherein the matrix-forming fluid contains a protein.
9. The method of claim 6 wherein cooling is by a method selected from the group consisting of immersing the chamber in a coolant, positioning the chamber in a bath through which a coolant can be circulated, and circulating a coolant within a jacketed chamber.
10. The method of claim 6 wherein said cooling rate effects a decrease in temperature from about 4°C to about -70°C in a time up to about two hours.

11. An apparatus for casting a biologically compatible matrix, said apparatus comprising

a matrix forming chamber forming an open box with five joined surfaces and a separate sixth surface attachable to said open box to form a  
5 closed box, the chamber capable of containing a matrix-forming fluid within spacers having a substantially uniform thickness between a top surface of a thermal conductive material and a bottom surface of a thermal conductive material,

a coolant chamber sized to contain said matrix-forming chamber  
10 on at least said top and bottom surfaces and having at least one fluid channel and at least one fluid port within each of said top and bottom surfaces, and fasteners to effect a liquid-tight seal among at least the five joined surfaces.

12. A method for producing a biocompatible matrix for a cultured skin device comprising

providing a matrix-forming fluid within gaskets having a substantially uniform thickness and defining a perimeter of a chamber, said  
5 gaskets positioned between a top thermally conductive surface in contact with said fluid and a bottom thermally conductive surface in contact with said fluid,  
freezing the fluid to form a solid sheet,  
dehydrating the solid sheet to form a biocompatible matrix, and  
physically crosslinking the matrix.

13. The method of claim 12 further populating the matrix with at least one animal cell.

14. A biocompatible matrix having substantially symmetric reticulations, said matrix prepared by
- providing a matrix-forming fluid to an apparatus wherein the fluid is contained between a first thermally conductive surface and a second
- 5 thermally conductive surface and has a substantially uniform thickness,
- cooling the fluid at a controlled rate to simultaneously remove heat from said first and second surfaces to form a solid sheet,
- dehydrating the solid sheet to form the matrix, and
- physically crosslinking the matrix,
- 10 said matrix capable of supporting cells inoculated thereon.
15. The matrix of claim 14 capable of supporting at least one epidermal cell and at least one dermal cell.
16. The matrix of claim 14 wherein the fluid contains a substance selected from the group consisting of a protein and a polypeptide.
17. The matrix of claim 21 wherein cooling is at a rate to effect a decrease in temperature from about 4°C to about -70°C at a time up to about two hours.

18. An apparatus for forming a biocompatible reticulated matrix comprising
- a bottom frame;
- a top frame having an undersurface of a thermally conductive
- 5 material,
- a center frame capable of being fastened between the bottom and top frames, the center frame having an oversurface of a thermally conductive material and capable of containing a matrix-forming fluid thereon within spacer gaskets capable of regulating a thickness of a matrix formed from said matrix-
- 10 containing fluid, and
- fasteners to fasten the bottom and top frames with the center frame there between,
- said apparatus capable of transferring heat at a rate to effect controlled freezing of the matrix-forming fluid to form the matrix.
19. The apparatus of claim 18 wherein the bottom frame comprises a framework forming a chamber capable of containing a coolant to effect freezing of the matrix-forming fluid.
20. The apparatus of claim 19 wherein the bottom frame further comprises at least two ports for providing the bottom frame with a coolant fluid and flowing the coolant fluid through the frame, and fasteners to fasten with the top frame.

21. The apparatus of claim 18 wherein at least one of the surfaces of a thermally conductive material is substantially non-adherent.
22. The apparatus of claim 18 wherein the thermally conductive material is a metal.
23. The apparatus of claim 18 wherein the spacer gaskets are of a resilient composition and contact the surfaces of thermal conductive materials.
24. The apparatus of claim 18 wherein at least one of the surfaces of thermal conductive materials has a non-adherent coating.
25. The apparatus of claim 18 wherein the top frame comprises a framework forming a chamber capable of containing a coolant fluid to effect freezing of the matrix-forming fluid.
26. The apparatus of claim 25 wherein the top frame further comprises at least two ports for filling the chamber with a coolant and flowing the coolant fluid through the apparatus, and fasteners to fasten with the bottom frame.

27. A method for producing a biocompatible matrix comprising providing a matrix-forming fluid comprising collagen between a first thermally conductive surface of a chamber and a second thermally conductive and within a perimeter defined by a gasket of substantially uniform thickness,
- cooling the matrix-forming fluid to form a solid uncrosslinked sheet having a substantially uniform thickness by freezing at a controlled rate, and dehydrating the solid sheet to form the matrix, and physically crosslinking the matrix.
28. The method of claim 27 wherein the physical crosslinking of the matrix is by a method selected from the group consisting of thermal dehydration, gamma irradiation, and combinations thereof.
29. The method of claim 27 further comprising sterilizing the crosslinked matrix.
30. The method of claim 27 wherein the first and second surfaces are substantially flat and substantially non-deformable.
31. The method of claim 27 wherein cooling is by a method selected from the group consisting of immersing the chamber in a static coolant fluid, placing the chamber in a coolant fluid which can be circulated, and circulating a coolant fluid within a coolant chamber.

32. The method of claim 27 wherein said matrix has a thickness and contains substantially uniform and substantially symmetric reticulations across said thickness.

33. An apparatus for casting a biologically compatible matrix, said apparatus comprising a metal chamber forming an open chamber with five joined surfaces and a separate sixth surface attachable to said open chamber to form a closed chamber containing a matrix-forming fluid,

5 spacers to space the first and second surfaces and thereby regulate a thickness of a matrix resulting from freezing of the matrix-forming fluid, and

fasteners to effect a liquid-tight seal among at least the five joined surfaces.

34. The apparatus of claim 33 further comprising at least one aperture throughout a length of the first surface and at least one aperture throughout a length of the second surface for circulating a coolant throughout the lengths of the top, bottom, and center frames.

35. A method for producing a biocompatible matrix for a replacement skin device comprising
- providing a collagen-containing matrix-forming fluid between a first thermally conductive surface of a closed chamber and a second thermally
- 5 conductive surface of the closed chamber,
- freezing the sheet to form a solid uncrosslinked sheet having a substantially uniform thickness,
- dehydrating the solid sheet to form the matrix, and
- physically crosslinking the matrix,
- 10 said matrix capable of supporting a lamination layer of cultured dermal cells for a layer of cultured epidermal cells applied thereon.

36. A biocompatible matrix having substantially uniform and substantially symmetric reticulations, said matrix prepared by providing a matrix-forming fluid to an apparatus wherein the fluid is contained between a first thermally conductive surface and a second thermally conductive surface and within a perimeter defined by a gasket of substantially uniform thickness,
- cooling the fluid at a controlled rate to simultaneously remove heat from said first and second surfaces form a solid sheet having a substantially uniform thickness,
- 5 10 dehydrating the solid sheet to form the matrix, and physically crosslinking the matrix,  
said matrix capable of supporting cells inoculated thereon.
37. The matrix of claim 36 capable of supporting at least one animal cell.
38. The matrix of claim 36 wherein the fluid further comprises a carbohydrate.
39. The matrix of claim 36 wherein cooling is at a rate to effect a decrease in temperature from about 4°C to about -70°C in a time up to about two hours.

40. An apparatus for controlled rate freezing of a matrix-forming fluid comprising a closed chamber defined by at least a top and bottom surface of a heat conductive material, said chamber containing said fluid, said heat conductive material symmetrically removing heat.

41. The apparatus of claim 40 wherein the chamber is a bladder.

42. The apparatus of claim 40 wherein the chamber further comprises at least one gasket of substantially uniform thickness separating said top and bottom surfaces.